this Response. No new matter has been added to the application.

Claim 74 has been amended so that it depends upon Claim 22. It is requested that the objection to Claim 74 be withdrawn and that claim 74 be considered at this time.

The Examiner has noted that an Abstract is required in this application. An Abstract has been attached to this Response on a separate page. It is requested that this objection be withdrawn.

Claims 22-73 have been rejected under 35 U.S.C. 112, first paragraph, as containing matter that was not adequately described in the specification. Claims 68, 70, 73 and 74 have been amended in response to the Examiner's objections. Claim 73 and claim 74 are now dependent on claim 22. It is submitted that this rejection is not well taken in light of the above amendments.

It is also submitted that complete structures are now shown in amended claims 68 and 70. Support for the amendments to claims 68 and 70 may be found in the specification on page 1, lines 26-35, page 5, lines 13-26, and in the exemplified compounds shown on pages 29 and 30 of the specification. The amended structures also show the position of the implied hydrogen atom at the chiral center.

Additionally, Claim 22 has been amended to delete the "proviso" objected to by the Examiner under 35 U.S.C. § 112, first paragraph. It is submitted that any reference to or any definition of substituents R', Ar' and Ar'R' has been removed from claim 22. In the amended claim, the definition of Y is now limited to the scope recited in the claims as originally filed. Therefore, in the newly amended claim Y is defined in accordance with the

original definition of optional substituents of Y, being R, ArR- and X. In the event that R_8 is hydrogen, the optional substituents on Y are limited to substituents within the original definition of R and Ar. Therefore, the amendment does not constitute "new matter."

It is also submitted that the definition of Y in amended claim 22 relates to subject matter which is described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors had at the time the application was filed possession of the claimed invention. It is submitted that the amendment merely limits the scope of the alternate embodiments of Y and optional substituents R, ArR- and X described in the description at page 2, line 24 - page 3, line 15. These definitions are in the nature of a Markush formulation. The elements of the formula are described and claimed as alternate elements. Thus, some alternates may be explicitly excluded from the claims without generating "new matter." As support for this position, Applicant relies upon the decision of the U.S. Court of Customs and Patent Appeals in In re: Driscoll, 195 USPQ 434 (1977) which held that an amendment to limit the scope of a Markush claim did not constitute new matter since the reader would have understood that the specification described various alternate embodiments and the amendment simply limited the number of embodiments that fell within the claims.

The Examiner also took the position that "the relative positions of the remaining two groups is not specified, so the chiral carbon could be either "R" or "S"; it cannot be determined." It is submitted that the "R" or "S" designations can only be applied once the four groups bonded to the chiral carbon atom are defined. However, it is also submitted

that the "R" and "S" designations are only labels that define the stereochemistry of a particular chiral carbon atom. It is also submitted that these labels do not define any physical property of the molecule containing the atom. A person of skill in the art would be capable of interpreting the structures in claims 68 and 70 to define the absolute configurations at the chiral carbon. As the Examiner is aware, a 4-coordinate sp^3-hybridized carbon atom (C*) forms bonds to its substituents (Sub) in a tetrahedral configuration, i.e., each Sub^1-C*-Sub^2 angle is 109.5°. In order to define the absolute configuration of a chiral carbon atom, it is only necessary to pictorially define the positions of three of the four bonds, because the geometric constraints imposed by tetrahedral geometry require that the fourth bond must be in the final open position. Nevertheless, in an attempt to advance prosecution, the amended structures for claims 68 and 70 define the positions of all four bonds for the chiral carbons in question, thereby defining the absolute configurations of the chiral carbon atoms.

One group in each of the claims is shown as coming out of the plane of the page (solid wedge) and another is shown as extending behind the plane of the page (H atom - broken wedge). The remaining two groups are in the plane of the page (line representations of the bonds). In the Office Action, the Examiner suggested that "the relative position of the remaining two groups is not specified." However, it is submitted that these groups are <u>not</u> interchangeable as they are now drawn. Thus the absolute configuration of the chiral carbon is specified. It is submitted that whether or not the chiral atoms in claims 68 and 70 can be labeled as being in the "R" or "S" configuration is not

relevant, because the absolute configuration of the structures as drawn is defined, without the need for an "R" or "S" label. Therefore, it is requested that the rejection be withdrawn for these reasons.

The typographical error in variable R_{11} in claim 22 has been corrected in accordance with the Examiner's request. Applicant has also corrected the typographical error regarding the duplication of "-NRCH(R_{11})COOH" in Claim 22. The first "-NRCH(R_{11})COOH" has been replaced with "-NHCH(R_{11})COOH." Support for this amendment may be found in the specification on page 3, line 19.

Additionally, Claims 22-73 have been rejected under 35 U.S.C. 112, second paragraph, as indefinite. It is submitted that the above comments made in regards to the rejection under 35 U.S.C. 112, first paragraph, and the amendments made to the claims themselves are sufficient to overcome the rejection and it is requested that it be withdrawn as well.

Claims 22-26, 60, 62, and 68-70 have been rejected under 35 U.S.C. 102(e) as anticipated by Webber (U.S. Patent No. 6,214,799). It is submitted that this rejection is not well taken.

It is submitted that the amendments made to the claims and the previously presented arguments also overcome this rejection. It is further submitted that the compounds taught by Webber do not satisfy all of the elements of newly amended claim 22, in particular, the newly amended definition of Y. Therefore, it is requested that the rejection be withdrawn in view of the amendments made to claim 22.

If it is believed that the application is not in condition for allowance, it is respectfully requested that the undersigned attorney be contacted at the telephone number below.

In the event this response is not considered to be timely filed, Applicants hereby petition for an appropriate extension of time. The fee for this extension may be charged to our Deposit Account No. 01-2300, referring to client-matter number 108281-00000, along with any other fees which may be required with respect to this application.

Respectfully submitted,
Arent Fox Kintner Plotkin & Kahn, PLLC

D. Daniel Dzara, II
Registration No. 47,543

1050 Connecticut Avenue, N.W., Suite 400
Washington, D.C. 20036-5339

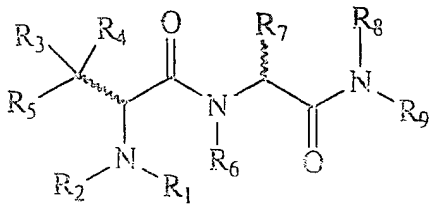
(202) 857-6000

DDD/ksm

Attachments: Petition for Extension of Time (2 Months)
Marked Up Copy of the Claims
Abstract

MARKED UP COPY OF THE CLAIMS

22. (Once Amended) A compound or pharmaceutically acceptable salt thereof, having the formula:



I

wherein:

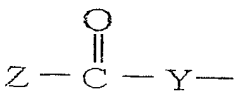
R_1 and R_2 are independently selected from the group consisting of H, R, and ArR-, or R_1 and R_2 are joined to form a ring;

R_3 and R_4 are independently selected from the group consisting of H, R, and ArR-, or R_3 and R_4 are joined to form a ring;

R_5 is selected from the group consisting of H, R, ArR-, and Ar;

R_6 is selected from the group consisting of H, R, and ArR-;

R_7 and R_8 are independently selected from the group consisting of: H, R, and ArR-; and

R_9 is:  ;

R is a saturated or unsaturated moiety having a linear, branched, or non-aromatic cyclic skeleton containing one to ten carbon atoms, zero to four nitrogen atoms, zero to four oxygen atoms, and zero to four sulfur atoms, and the carbon atoms are optionally substituted with: =O, =S, -OH, -OR_{10}, -O_2CR_{10}, -SH, -SR_{10}, -$SOCR_{10}$, -NH_2, -NHR_{10}, -$N(R_{10})_2$, -$NHCOR_{10}$, -$NR_{10}COR_{10}$, -I, Br, -C1, -F, -CN, -CO_2H, -CO_2R_{10}, -CHO, -COR_{10}, -$CONH_2$, -$CONHR_{10}$, -$CON(R_{10})_2$, -COSH, -$COSR_{10}$, -NO_2, -SO_3H, -SOR_{10}, -SO_2R_{10}, wherein R_{10} is a linear, branched or cyclic, one to ten carbon atom saturated or unsaturated alkyl group;

the ring formed by joining R_1 and R_2 or by joining R_3 and R_4 is a three to seven member non-aromatic cyclic skeleton within the definition of R,

X is a moiety selected from the group consisting of -OH, -OR, =O, =S, -O_2CR, -SH, -SR, -SOCR, -NH_2, -NHR, -$N(R)_2$, -NHCOR, -NRCOR, -I, -Br, -Cl, -F, -CN, -CO_2H, -CO_2R, -CHO, -COR, -$CONH_2$, -CONHR, -$CON(R)_2$, -COSH, -COSR, -NO_2, -SO_3H, -SOR, and -SO_2R;

Ar is an aromatic ring selected from the group consisting of phenyl, naphthyl, anthracyl, phenanthryl, furyl, pyrrolyl, thiophenyl, benzofuryl, benzothiophenyl, quinolinyl, isoquinolyl, imidazolyl, thiazolyl, oxazolyl, and pyridinyl, optionally substituted with R or X;

Y is a linear, unsaturated, two to six carbon atom alkyl group, optionally substituted with R, ArR-, or X, provided however if R8 is H, then the optional substituents on Y are

limited to R and ArR- wherein R is linear, branched or cyclic alkyl of one to ten carbon atoms and Ar is phenyl, napthyl, anthracyl, or phenanthryl; and,

Z is a moiety selected from the group consisting of: -OH, -OR; -SH; -SR; $-NH_2$; [$-NRCH(R_{ll})COOH$] $-NHCH(R_{11})COOH$; and $-NRCH(R_{11})COOH$, wherein R_{11} is a moiety having the formula: R, or $-(CH_2)_nNR_{12}R_{l3}$, wherein n=1-4 and R_{12} and R_{13} are independently selected from the group consisting of H; R; and $-C(NH)(NH_2)$[;

and wherein:

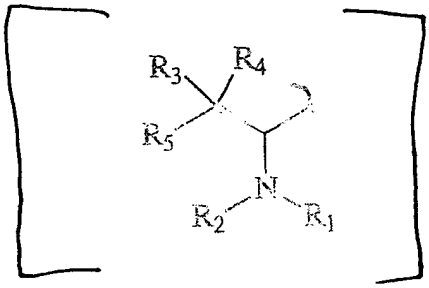
if R_8 is H, Y may only be substituted with R' or Ar'R'-, in which

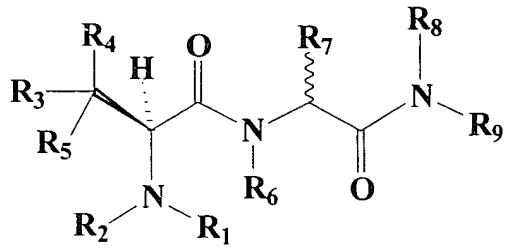
R' is a saturated linear, branched, or cyclic skeleton containing one to ten carbon atoms, and

Ar' is an aromatic ring selected from the group consisting of phenyl, napthyl, anthracyl and phenanthryl, optionally substituted with R']

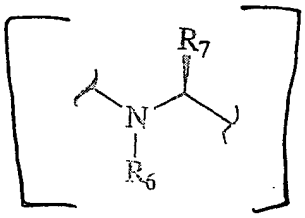
or pharmaceutically acceptable salt thereof.

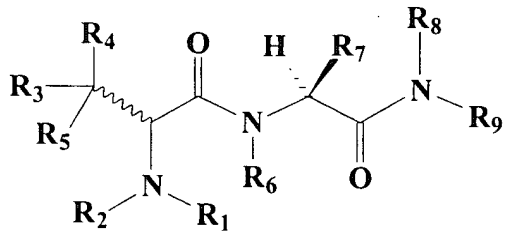
68. (Once Amended) The compound of claim 22, having the configuration:





70. (Once Amended) The compound of claim 22, having the configuration:





73. (Once Amended) A pharmaceutical composition suitable for treating tumors comprising an anti-tumor effective amount of at least one compound of claim [1] 22 and acceptable pharmaceutical excipient.

74. (Once Amended) A method of treating tumors by arresting cell mitosis in a patient in need of such treatment comprising administering to said patient an anti-mitotic effective amount of at least one compound of claim [1] 22.